

## **REMARKS**

In the Office Action Summary, the Examiner indicates that claims 29-32 and 39-41 are pending in this application, claims 29-32 are rejected and claims 39-41 are withdrawn from consideration. Applicants submit that the Office Action Summary is in error. In fact, in the instant application, claims 29-32 and 39-43 are pending. Furthermore, in the Restriction Requirement issued by the Examiner on October 13, 2006, claim 39 was assigned in the same Group as claims 29-32 rather than claims 40-43. In response to the undersigned attorney's phone message regarding this issue on June 13, 2007, the Examiner left the undersigned attorney a message June 14, 2007, stating that the Office Action Summary is in error, actually all the pending claims 29-32 and 39-41 were examined on the merit and no claim was withdrawn from consideration. Thus, in the present application, claims 29-32 and 39-43 are pending and rejected. In view of the forgoing amendment and the following remarks, reconsideration and withdrawal of the present basis for rejection the claims herein of the application are respectfully requested.

### **I. Discussion of the Amendment**

Claim 29 has been amended to delete the definitions of  $X^1$ ,  $R^4$ ,  $R^{4'}$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{15}$  and  $R^{16}$ , and narrow the definitions of W, Y, Z, A, B, D, E, R,  $R^0$ ,  $R^1$ , X,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ , c, d, e, f, g, and h as following:

W is  $R^1$ -A-C( $R^{13}$ );

Y is carbonyl;

Z is N( $R^0$ );

A is phenylene or phenylenemethyl;

B is a bivalent methylene or ethylene radical which is substituted by a radical from the group consisting of (C<sub>1</sub>-C<sub>8</sub>)-alkyl and (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl;

D is C( $R^2$ )( $R^3$ );

E is  $R^{10}$ CO;

R is hydrogen, methyl or ethyl;

$R^0$  is optionally substituted (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl;

$R^1$  is X-NH-C(N=H), X-NH-C(=NX)-NH or X-NH-CH<sub>2</sub>;

X is hydrogen;

$R^2$  is hydrogen or (C<sub>1</sub>-C<sub>8</sub>)-alkyl;

$R^3$  is optionally substituted (C<sub>6</sub>-C<sub>14</sub>)-aryl,  $R^{11}$ NH, CON(CH<sub>3</sub>) $R^{14}$  or CONHR<sup>14</sup>;

$R^5$  is optionally substituted (C<sub>6</sub>-C<sub>14</sub>)-aryl, wherein the aryl radical can be mono- or polysubstituted by identical or different radicals from the group consisting of (C<sub>1</sub>-C<sub>18</sub>)-alkyl, and halogen;

$R^{10}$  is hydroxyl or (C<sub>1</sub>-C<sub>8</sub>)-alkoxy;

R<sup>11</sup> is R<sup>12</sup>CO;

R<sup>12</sup> is (C<sub>1</sub>-C<sub>10</sub>)-alkoxy;

R<sup>13</sup> is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)-alkyl;

R<sup>14</sup> is (C<sub>1</sub>-C<sub>10</sub>)-alkyl which is substituted by a radical from the group consisting of hydroxycarbonyl and (C<sub>1</sub>-C<sub>8</sub>)-alkoxycarbonyl and can optionally be substituted by a radical R<sup>5</sup>;

c and d are 1;

f and g are 0; and

e and h independently of one another are 0 or 1.

Claim 29-32, 40 and 42-43 are also amended to better and more clearly reflect what Applicants regard as their invention.

Claims 39 and 41 are canceled, without prejudice.

Applicants reserve their right to pursue any canceled or deleted subject matter by a subsequent application.

This amendment does not add any new matter.

## II. Discussion of the Written Description Rejection

The Examiner indicates that claims 29-32 and 39-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as the claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention. Specifically, the Examiner alleges that

"Claims are drawn to a large group of compounds of formula I where there is no core structure. All the substituents are variables. The method of treating a disease or disorder involving inflammation and method of antagonizing VL-4, treating disease or disorder from rheumatoid arthritis, tumor growth (various diseases listed in claim 42 and 43) by the thousands of compounds was not possessed by Applicants at the time application was filed."  
Office Action, page 4.

Applicants respectfully traverse the instant rejection.

Applicants submit that the Examiner's rejection is improper as claims 29-32 and 39-43 indeed comply with the written description requirement. The first paragraph of 35 U.S.C. § 112 requires an applicant to convey with reasonable clarity to those skilled in the art that, as of the filing date, the applicant was in possession of the claimed invention. In the present application, claims 29-32 and 39-43 are directed to compounds of formula Id and their use as VLA-4 antagonists. Applicants submit that there is ample basis throughout the specification for Applicants claiming their invention as described in claims 29-32 and 39-43. In the specification, Applicants provide clear definition of all the variables in formula Id, and particular/preferred

embodiments of the invention. More importantly, the specification exemplifies a considerable number of species that are within the scope of formula Id.

Furthermore, the present application, at page 48, last paragraph to page 50, first paragraph, describes the usefulness of the compounds of formula Id in the treatment of pathologies, in which VLA-4 receptor plays a role, specifically in the therapeutic and/or preventive treatment of various diseases including those diseases claimed in claims 40 and 42-43. Thus, the originally-filed specification clearly describes the complete conception of the invention of claims 29-32 and 39-43, and it conveys with reasonable clarity to those skilled in the art that, as of the filing date, Applicants were in possession of the claimed invention as described in claims 29-32 and 39-43. This is all that is necessary under the written description requirement of 35 U.S.C. § 112, first paragraph.

Nevertheless, in order to advance the prosecution of the present application, claim 29 has been amended to a narrower scope to encompass only some particular/preferred embodiments described in the specification and Examples 50-54, 62, 74 and 75. The compounds of the amended claim 29 have clear core structures and limited variabilities on the substituents. Claims 39 and 41 are canceled, without prejudice. Thus, in view of the forgoing amendment and the arguments presented above, it is submitted that the instant rejection is overcome, and claim 29-32, 40 and 42-43 are allowable.

### **III. Discussion of the Enablement Rejection**

Claims 29-32 and 39-43 are rejected under 35 U.S.C. §112, first paragraph, as the Examiner alleges,

“because the specification, while being enabling for certain compounds and method of use does not reasonably provide enablement of large group of compounds of formulas I where there is no core structure and the substituents are variables. The method of treating a disease or disorder involving inflammation and method of antagonizing VL-4, treating disease or disorder from rheumatoid arthritis, tumor growth (various diseases listed in claim 42 and 43) by the thousands of compounds.

The specification does not enable any person skilled in the art to which it pertains, or with which is most nearly connected, to make and/or use the invention commensurate in the scope with these claims.”  
Office Action, page 10.

Applicants respectfully traverse the instant rejection.

First, Applicants would like to point out that although the Examiner recognizes the specification “being enabling for certain compounds and method of use”, she fails to provide any specific guidance as to the scope of Applicants’ invention that she believe is enabled, except merely stating that Example 50 is allowable. Applicants respectfully request clarification on this point.

Applicants submit that the amended claims 29-32, 40 and 42-43 are enabled by the specification. The first paragraph of 35 U.S.C. § 112 requires that the specification enables a person skilled in the art to make and/or use the claimed invention without undue experimentation. Claim 29

has been amended to a narrower scope to encompass only some particular/preferred embodiments described in the specification and Examples 50-54, 62, 74 and 75. The compounds of the amended claim 29 have clear core structures and limited variabilities on the substituents. The specification exemplifies preparation of Examples 50-54, 62, 74 and 75, and a considerable number of compounds having similar chemical structures. A person of ordinary skill in the art would be able to follow the procedures described in those examples to prepare any compound of claims 29-31 without undue experimentation.

Furthermore, the specification, at pages 149-153, describes an assay that measures the activity of the compounds of present invention on the interaction between VCAM-1 and VLA-4, and numerous examples and their corresponding activities are clearly present in the specification. In addition, potent antagonists for VLA-4 receptor would be considered useful in the treatment of any pathology in which VLA-4 receptor is involved, such as the diseases listed in the specification and claimed in claims 40 and 42-43. Thus, a person of ordinary skill in the art would be able to follow the assay described in the specification to measure the activity of any compound of claims 29-31 and practice the invention as claimed in claims 40 and 42-43 without undue experimentation.

In view of the aforesaid, the specification is enabling for making and/or using the invention commensurate in scope with claims 29-32, 40 and 42-43. Claims 39 and 41 have been canceled, without prejudice. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

#### **IV. Conclusion**

In view of the above remarks, the present application is in condition for allowance. Early notice to this effect is, thus, respectfully requested.

The Commissioner is hereby authorized to charge the fee required and any additional fees that may be needed to Deposit Account No. **18-1982** in the name of Aventis Pharmaceuticals Inc.

Respectfully submitted,



---

Jiang Lin, Reg. No. 51,065  
Attorney for Applicants

Date: June 15, 2007

sanofi-aventis U.S. LLC  
Patent Department  
Route #202-206 / P.O. Box 6800  
Bridgewater, NJ 08807-0800  
Telephone (908) 231-3582  
Telefax (908) 231-2626

sanofi-aventis Docket No. DEAV1996/F306 US CNT